INTRODUCTION. Riboswitches are structured RNAs usually located in the untranslated regions of bacterial mRNAs that bind metabolites and control gene expression (1). Each riboswitch typically senses one metabolite and functions as a simple genetic switch usually by controlling transcription termination or translation initiation. However, the structures and functions of riboswitches can be more complex, and recent findings that expand our understanding of the complexity of riboswitches will be presented.

METHOD. New riboswitch classes are being discovered by comparative sequence analysis (2). RNA structures that are conserved amongst a variety of species and that are commonly associated with metabolic genes are excellent riboswitch candidates. Each candidate can be assessed by biochemical and genetic assays to confirm that the RNAs selectively bind metabolites in the absence of proteins and that this binding leads to gene regulation.

RESULTS. Several recent discoveries indicate that riboswitches can use a diversity of RNA folds to achieve the levels of molecular recognition required to serve as precision sensors in modern cells (e.g. 3). Furthermore, riboswitch architectures have been identified that allow RNA gene control systems to exhibit properties such as cooperative ligand binding (4), two-input sensory responses (5), and more “digital” gene control characteristics (6). Recently (7,8), we have determined that riboswitches in eukaryotes control the expression of genes by regulating splicing and RNA processing events (e.g. Fig. 1), which expands the types of gene control mechanisms known to be used by riboswitches beyond the regulation of transcription termination and translation initiation.

DISCUSSION. Many of the known riboswitch classes are widely distributed amongst bacterial species, suggesting that some of these RNAs are of ancient origin. However, since riboswitches persist in modern organisms, including eukaryotes, they must be capable of efficiently sensing metabolites and controlling gene expression, or they would have been displaced by genetic factors made of protein. The diversity of riboswitch aptamer types and the diversity of
mechanisms used by these molecular switches to control gene expression demonstrate the enormous structural and functional potential of RNA.

Fig. 1. Fungal gene regulation by a riboswitch that controls alternative splicing (7).

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REFERENCES